

β1a1

NcoI  
 -2 CCATGGGCAGAGACTCCCCAAGGGATTTCGTGTACCAGTTCAAGGGCCTGTGCTACTACACC 60  
 M G R D S P R D F V Y Q F K G L C Y Y T  
 61 AACGGGACGCAGCGCATAACGGGATGTGATCAGATACATCTACAACCAGGAGGAGTACCTG 120  
 N G T Q R I R D V I R Y I Y N Q E E Y L  
 121 CGCTACGACAGCGACGTGGGCGAGTACCGCGCGCTGACCGAGCTGGGGCGGCCCTCAGCC 180  
 R Y D S D V G E Y R A L T E L G R P S A  
 181 GAGTACTTTAACAAGCAGTACCTGGAGCAGACGCGGGCCGAGCTGGACACGGTCTGCAGA 240  
 E Y F N K Q Y L E Q T R A E L D T V C R  
 241 CACAACTACGAGGGGTCGGAGGTCCGCACCTCCCTGCGGCGGCTTGGAGGTCAAGACGAC 300  
 H N Y E G S E V R T S L R R L G G Q D D  
 301 ATTGAGGCCGACCACGTAGCCGCCTATGGTATAAATATGTATCAGTATTATGAATCCAGA 360  
 I E A D H V A A Y G I N M Y Q Y Y E S R  
 361 GGCCAGTTTACACATGAATTTGATGGTGACGAGGAATTCTATGTGGACTTGGATAAGAAG 420  
 G Q F T H E F D G D E E F Y V D L D K K  
 421 GAGACCATCTGGAGGATCCCCGAGTTTGGACAGCTGACAAGCTTTGACCCCCAAGGTGGA 480  
 E T I W R I P E F G Q L T S F D P Q G G  
 481 CTTCAAAATATAGCTATAATAAAACACAATTTGGAAATCTTGATGAAGAGGTCAAATTCA 540  
 L Q N I A I I K H N L E I L M K R S N S  
 541 ACCCAAGCTGTCAACTAACTCGAG  
 T Q A V N end

FIG. 1A

FIG. 1B

$\beta 1\alpha 1$ /MBP-72-89

NcoI

CCATGGGCAGAGACTCCCCACAGAGAGAGCCAGAGGACTCAGGATGAGAACCCAGTGGTGCACCTTCGGAGGTGGAGGCTCACTAGTGGCCCCGAGGCTCT

M G R D S P Q K S Q R T Q D E N P V V H F G G G S L V P R G S

GGAGTGGAGGCTCC

G G G G S

SpeI

-----thrombin-----|

FIG. 1C

$\beta 1\alpha 1$ /MBP-55-69

NcoI

CCATGGGCAGAGACTCCTCCGGCAGGATTGCGATCATGCGCGCGGACGACCCACTACGGTGGAGGTGGAGGCTCACTAGTG

M G R D S S G K D S H A A R T T H Y G G G G S L V

SpeI

FIG. 1D

$\beta 1\alpha 1$ /CM-2

NcoI

CCATGGGCAGAGACTCCAACTGGAACTGCAGTCCGCTCTCGAAGAGCTGAGCTTCCTGGAAACGAGGTGGAGGCTCACTAGTG

M G R D S K L E L Q S A L E E A E A S L E H G G G S L V

SpeI

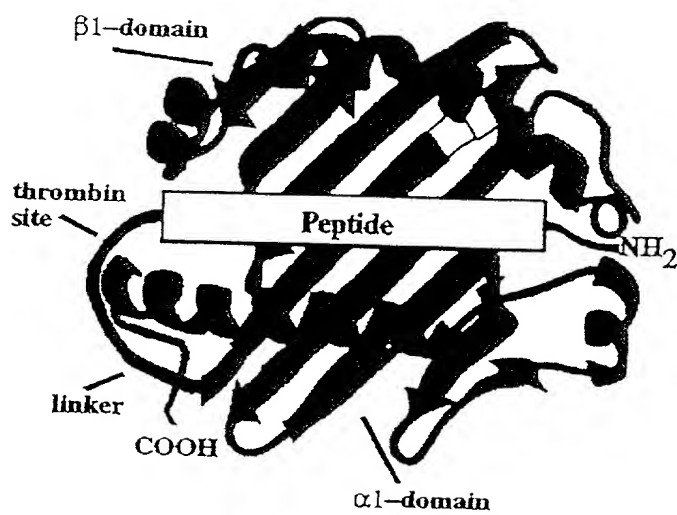


FIG. 2  
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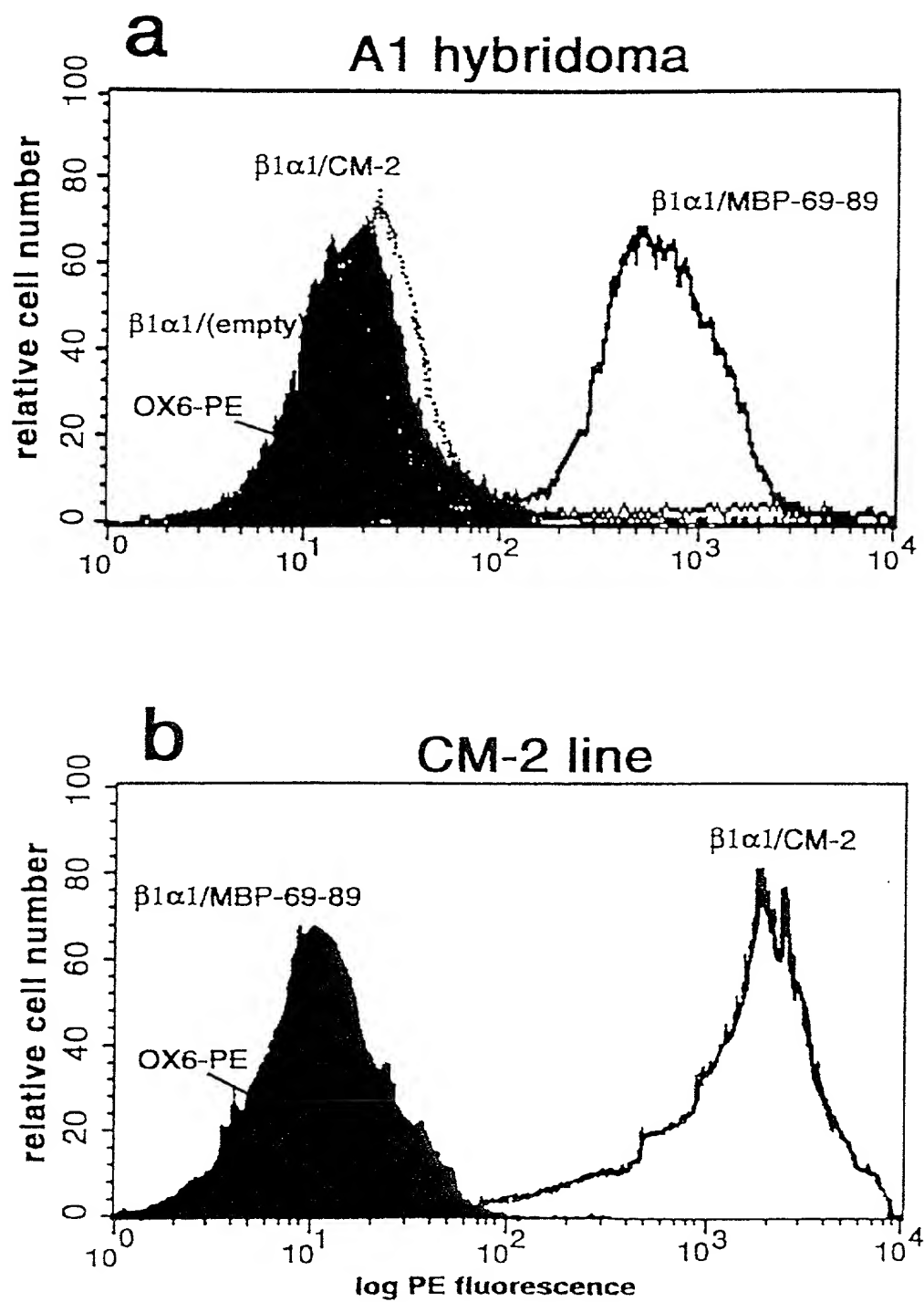


FIG. 3

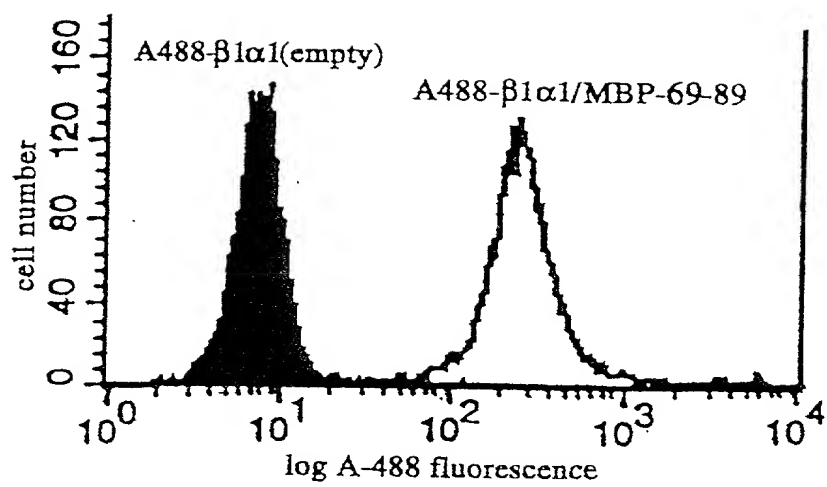


FIG. 4  
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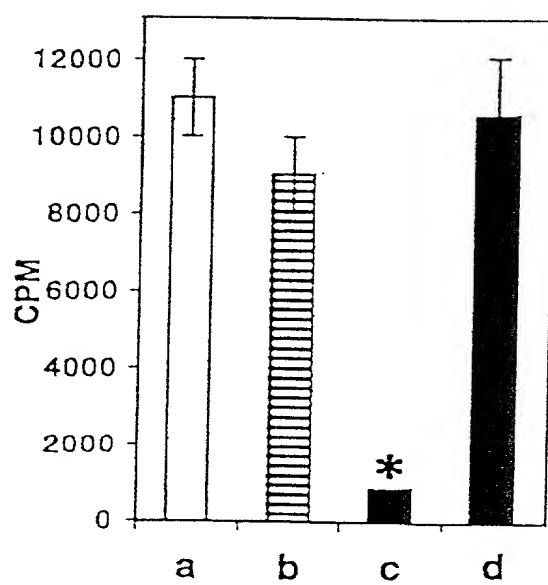


FIG. 5  
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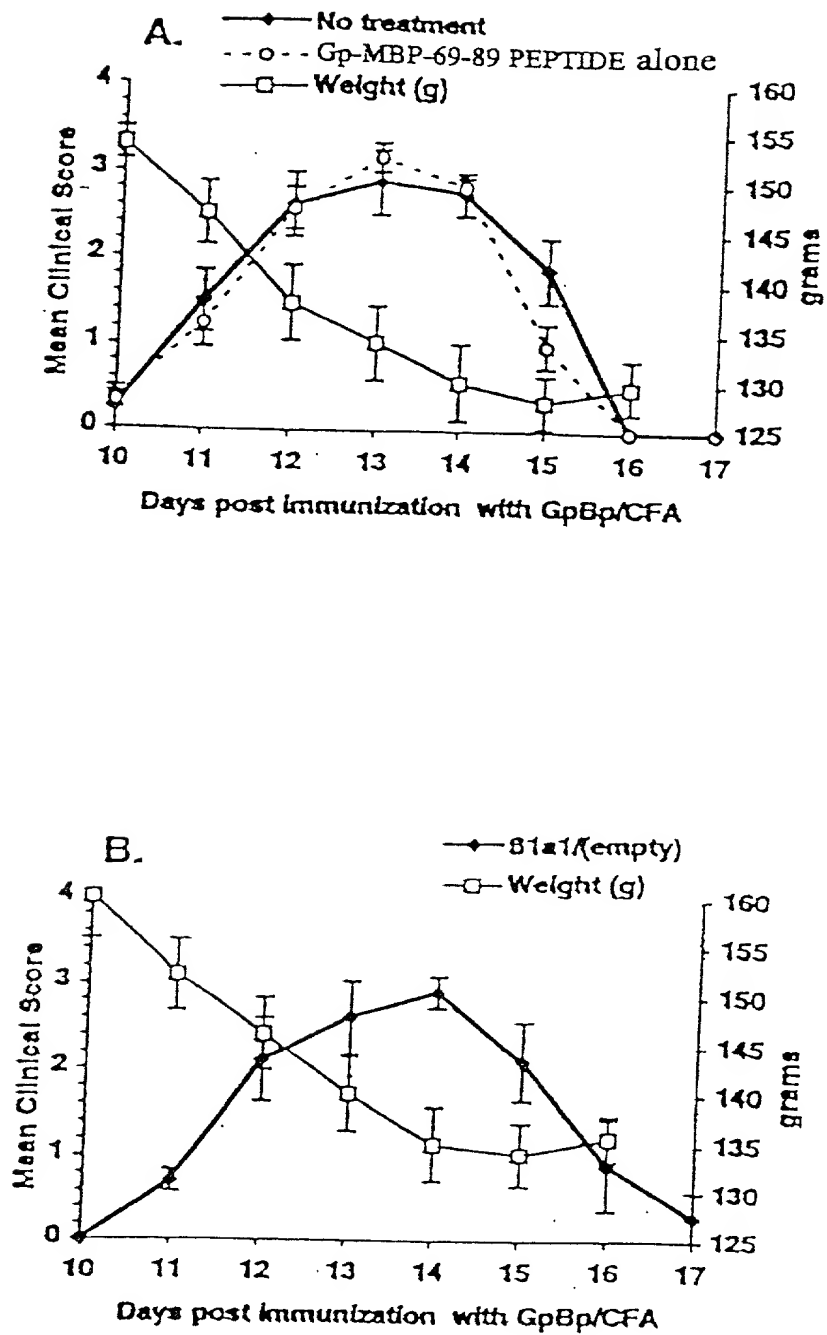


FIG. 6A  
7/15

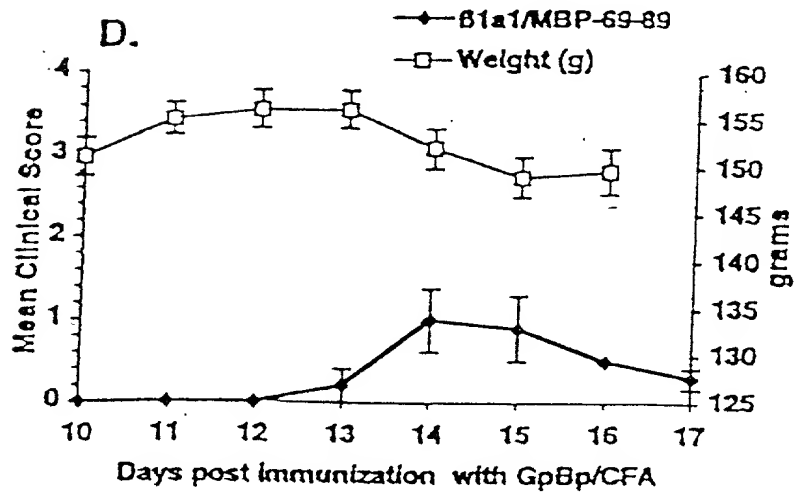
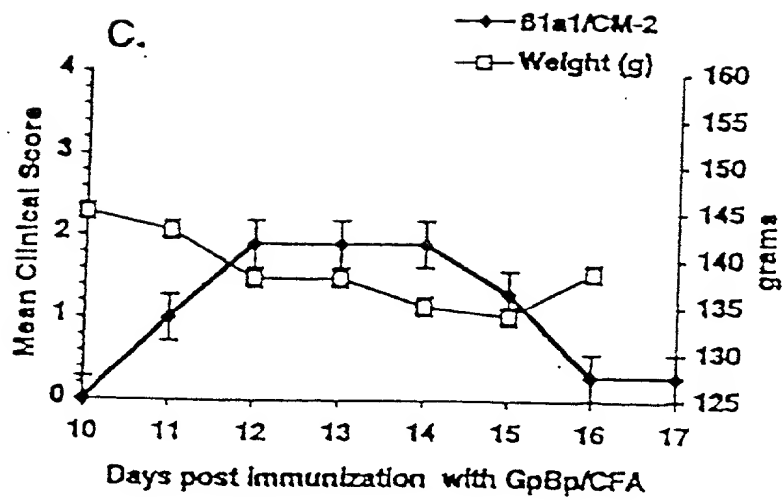


FIG. 6B  
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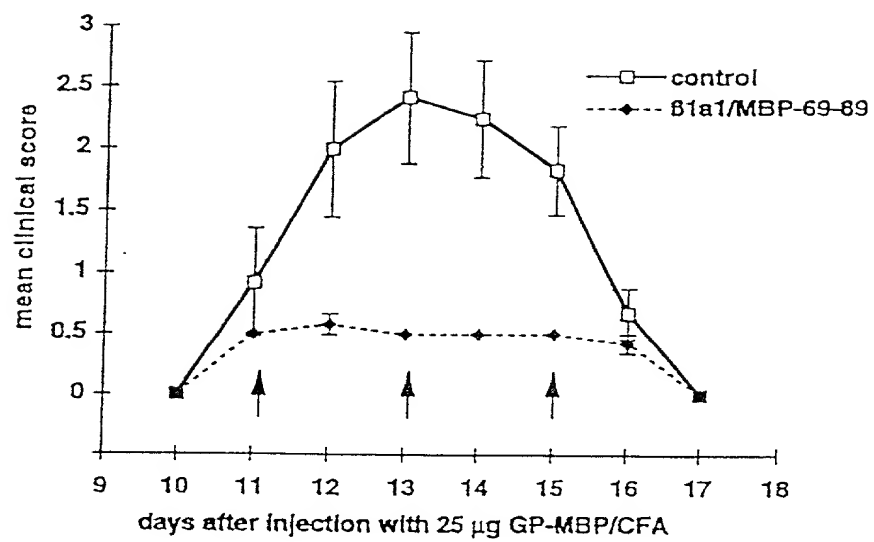


FIG. 7  
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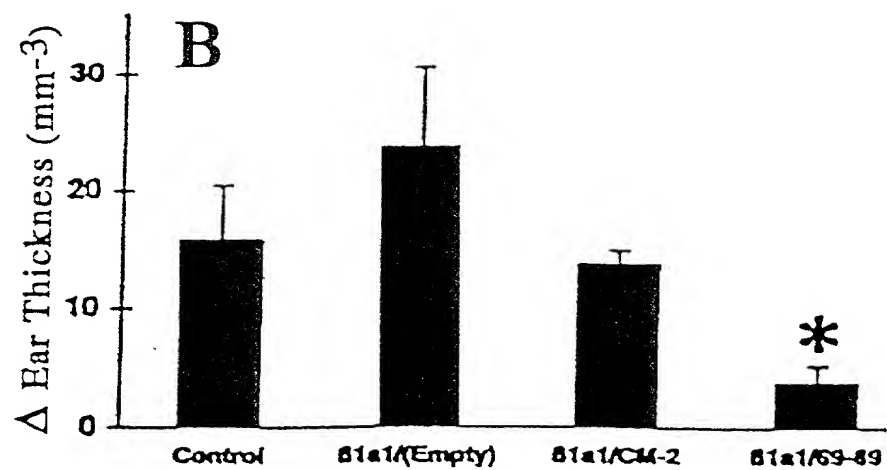
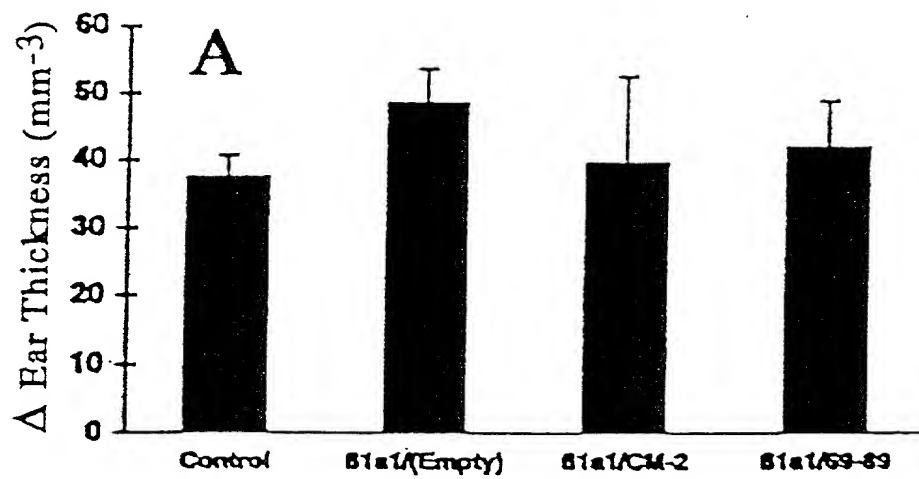


FIG. 8  
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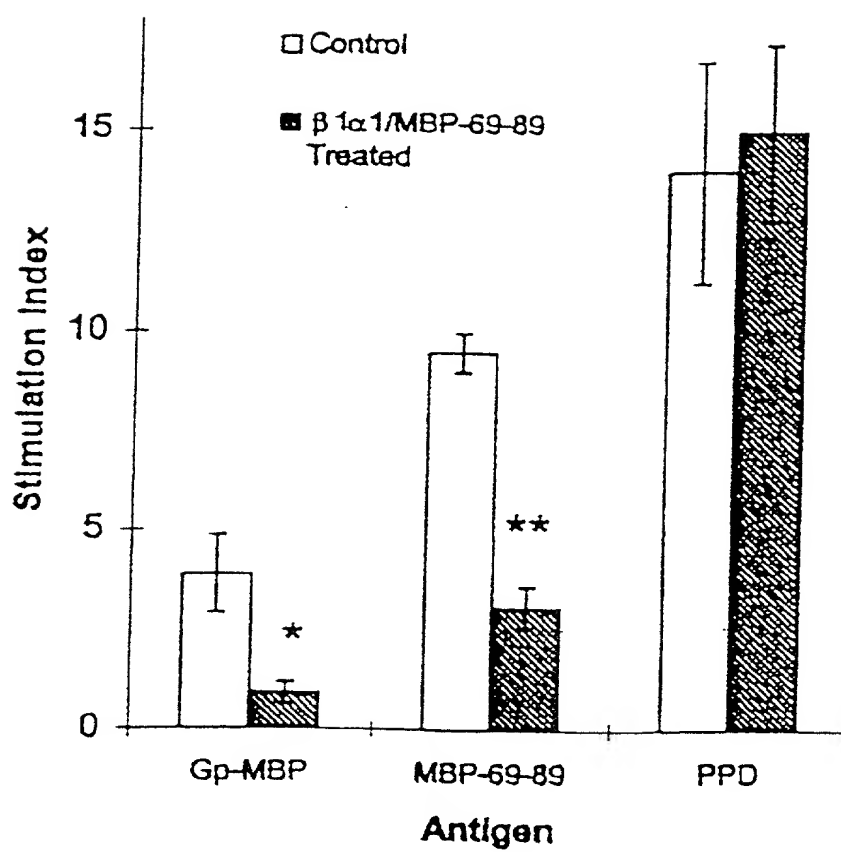


FIG. 9  
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$\beta$ 1 domain:  
 ARG4-PRO5-ARG6-PHE7-LEU8-TRP9-GLN10-LEU11-LYS12-PHE13-GLU14-CYS15-  
 HIS16-PHE17-PHE18-ASN19-GLY20-THR21-GLU22-ARG23-VAL24-ARG25-LEU26-  
 LEU27-GLU28-ARG29-CYS30-ILE31-TYR32-ASN33-GLN34-GLU35-GLU36-SER37-  
 VAL38-ARG39-PHE40-ASP41-SER42-ASP43-VAL44-GLY45-GLU46-TYR47-ARG48-  
 ALA49-VAL50-THR51-GLU52-LEU53-GLY54-ARG55-PRO56-ASP57-ALA58-GLU59-  
 TYR60-TRP61-ASN62-SER63-GLN64-LYS65-ASP66-LEU67-LEU68-GLU69-GLN70-  
 ARG71-ARG72-ALA73-ALA74-VAL75-ASP76-THR77-TYR78-CYS79-ARG80-HIS81-  
 ASN82-TYR83-GLY84-VAL85-GLY86-GLU87-SER88-PHE89-THR90-VAL91-GLN92-  
 ARG93-ARG94-VAL95

$\alpha$ 1 domain:  
 GLU3-GLU4-HIS5-VAL6-ILE7-ILE8-GLN9-ALA10-GLU11-PHE12-TYR13-LEU14-  
 ASN15-PRO16-ASP17-GLN18-SER19-GLY20-GLU21-PHE22-MET23-PHE24-ASP25-  
 PHE26-ASP27-GLY28-ASP29-GLU30-ILE31-PHE32-HIS33-VAL34-ASP35-MET36-  
 ALA37-LYS38-LYS39-GLU40-THR41-VAL42-TRP43-ARG44-LEU45-GLU46-GLU47-  
 PHE48-GLY49-ARG50-PHE51-ALA52-SER53-PHE54-GLU55-ALA56-GLN57-GLY58-  
 ALA59-LEU60-ALA61-ASN62-ILE63-ALA64-VAL65-ASP66-LYS67-ALA68-ASN69-  
 LEU70-GLU71-ILE72-MET73-THR74-LYS75-ARG76-SER77-ASN78-TYR79-THR80-  
 PRO81-ILE82-THR83-ASN84

FIG. 10A  
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$\beta$ 1 domain:  
 ARG4-PRO5-TRP6-PHE7-LEU8-GLU9-TYR10-CYS11-LYS12-SER13-GLU14-CYS15-  
 HIS16-PHE17-TYR18-ASN19-GLY20-THR21-GLN22-ARG23-VAL24-ARG25-LEU26-  
 LEU27-VAL28-ARG29-TYR30-PHE31-TYR32-ASN33-LEU34-GLU35-GLU36-ASN37-  
 ALA49-VAL50-THR51-GLU52-LEU53-GLY54-ARG55-PRO56-ASP57-ALA58-GLU59-  
 ASN60-TRP61-ASN62-SER63-GLN64-PRO65-GLU66-PHE67-LEU68-GLU69-GLN70-  
 LYS71-ARG72-ALA73-GLU74-VAL75-ASP76-THR77-VAL78-CYS79-ARG80-HIS81-  
 ASN82-TYR83-GLU84-ILE85-PHE86-ASP87-ASN88-PHE89-LEU90-VAL91-PRO92-  
 ARG93-ARG94-VAL95

$\alpha$ 1 domain:  
 GLU3-GLU4-HIS5-THR6-ILE7-ILE8-GLN9-ALA10-GLU11-PHE12-TYR13-LEU14-  
 LEU15-PRO16-ASP17-LYS18-ARG19-GLY20-GLU21-PHE22-MET23-PHE24-ASP25-  
 PHE26-ASP27-GLY28-ASP29-GLU30-ILE31-PHE32-HIS33-VAL34-ASP35-ILE36-  
 GLU37-LYS38-SER39-GLU40-THR41-ILE42-TRP43-ARG44-LEU45-GLU46-GLU47-  
 PHE48-ALA49-LYS50-PHE51-ALA52-SER53-PHE54-GLU55-ALA56-GLN57-GLY58-  
 ALA59-LEU60-ALA61-ASN62-ILE63-ALA64-VAL65-ASP66-LYS67-ALA68-ASN69-  
 LEU70-ASP71-VAL72-MET73-LYS74-GLU75-ARG76-SER77-ASN78-ASN79-THR80-  
 PRO81-ASP82-ALA83-ASN84

FIG. 10B  
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$\beta$ 1 domain:  
 MET (-2) -GLY (-1) -ARG1-ASP2-SER3-PRO4-ARG5-ASP6-PHE7-VAL8-TYR9-  
 GLN10-PHE11-LYS12-GLY13-LEU14-CYS15-TYR16-TYR17-THR18-ASN19-GLY20-  
 THR21-GLN22-ARG23-ILE24-ARG25-ASP26-VAL27-ILE28-ARG29-TYR30-ILE31-  
 TYR32-ASN33-GLN34-GLU35-GLU36-TYR37-LEU38-ARG39-TYR40-ASP41-SER42-  
 ASP43-VAL44-GLY45-GLU46-TYR47-ARG48-ALA49-LEU50-THR51-GLU52-LEU53-  
 GLY54-ARG55-PRO56-SER57-ALA58-GLU59-TYR60-TRP61-ASN62-SER63-GLN64-  
 LYS65-GLN66-TYR67-LEU68-GLU69-GLN70-THR71-ARG72-ALA73-GLU74-LEU75-  
 ASP76-THR77-VAL78-CYS79-ARG80-HIS81-ASN82-TYR83-GLU84-GLY85-SER86-  
 GLU87-VAL88-ARG89-THR90-SER91-LEU92-ARG93-ARG94-LEU95

$\alpha$ 1 domain:  
 ALA2-ASP3-HIS4-VAL5-ALA6-ALA7-TYR8-GLY9-ILE10-ASN11-MET12-TYR13-  
 GLN14-TYR15-TYR16-GLU17-SER18-ARG19-GLY20-GLN21-PHE22-THR23-HIS24-  
 GLU25-PHE26-ASP27-GLY28-ASP29-GLU30-GLU31-PHE32-TYR33-VAL34-ASP35-  
 LEU36-ASP37-LYS38-LYS39-GLU40-THR41-ILE42-TRP43-ARG44-ILE45-PRO46-  
 GLU47-PHE48-GLY49-GLN50-LEU51-THR52-SER53-PHE54-ASP55-PRO56-GLN57-  
 GLY58-GLY59-LEU60-GLN61-ASN62-ILE63-ALA64-ILE65-ILE66-LYS67-HIS68-  
 ASN69-LEU70-GLU71-ILE72-LEU73-MET74-LYS75-ARG76-SER77-ASN78-SER79-  
 THR80-GLN81-ALA82-VAL83-ASN84

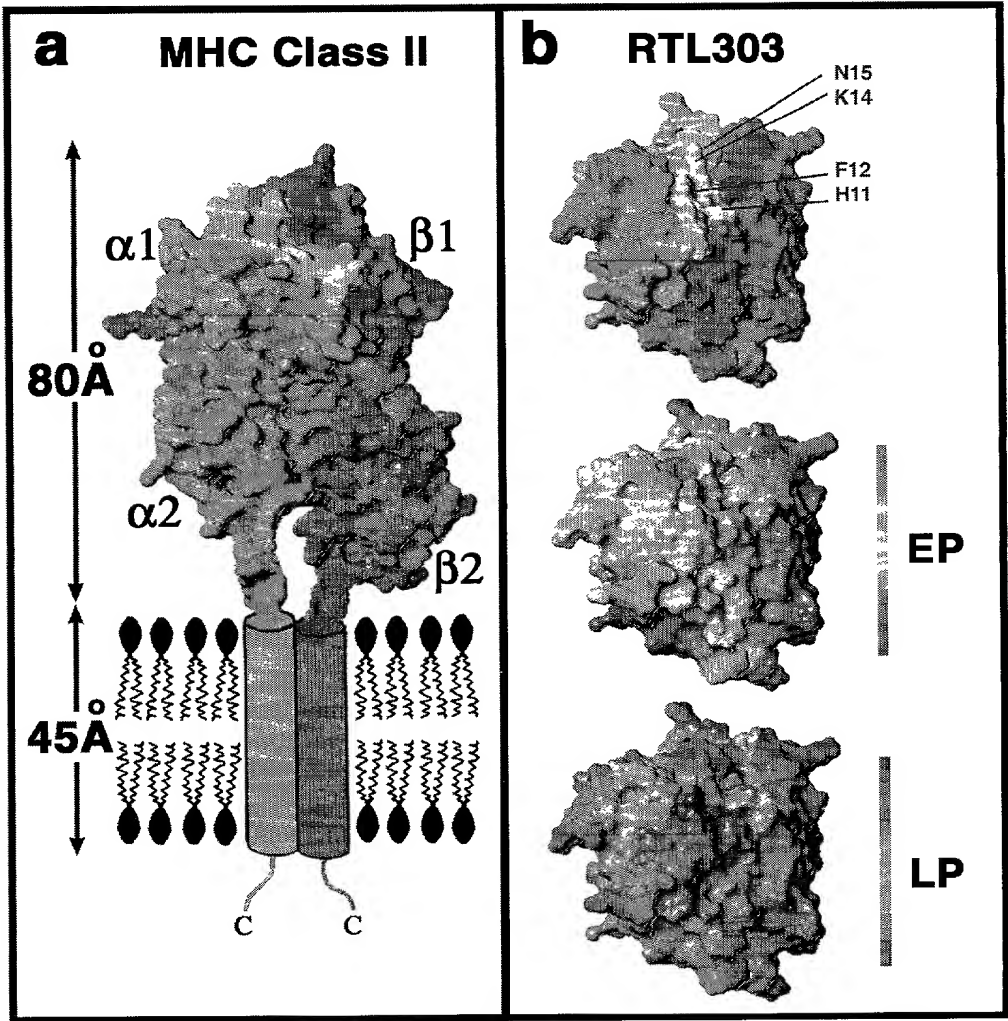
$\alpha 1$  domain:  
 GLY1-SER2-HIS3-SER4-MET5-ARG6-TYR7-PHE8-TYR9-THR10-ALA11-MET12-  
 SER13-ARG14-PRO15-GLY16-ARG17-GLY18-GLU19-PRO20-ARG21-PHE22-ILE23-  
 ALA24-VAL25-GLY26-TYR27-VAL28-ASP29-ASP30-THR31-GLN32-PHE33-VAL34-  
 ARG35-PHE36-ASP37-SER38-ASP39-ALA40-ALA41-SER42-PRO43-ARG44-THR45-  
 GLU46-PRO47-ARG48-PRO49-PRO50-TRP51-ILE52-GLU53-GLN54-GLU55-GLY56-  
 PRO57-GLU58-TYR59-TRP60-ASP61-ARG62-ASN63-THR64-GLN65-ILE66-PHE67-  
 LYS68-THR69-ASN70-THR71-GLN72-THR73-TYR74-ARG75-GLU76-ASN77-LEU78-  
 ARG79-ILE80-ALA81-LEU82-ARG83-TYR84-

$\alpha 2$  domain:  
 TYR85-ASN86-GLN87-SER88-GLU89-ALA90-GLY91-SER92-HIS93-ILE94-ILE95-  
 GLN96-ARG97-MET98-TYR99-GLY100-CYS101-ASP102-LEU103-GLY104-PRO105-  
 ASP106-GLY107-ARG108-LEU109-LEU110-ARG111-GLY112-HIS113-ASP114-  
 GLN115-SER116-ALA117-TYR118-ASP119-GLY120-LYS121-ASP122-TYR123-  
 ILE124-ALA125-LEU126-ASN127-GLU128-ASP129-LEU130-SER131-SER132-  
 TRP133-THR134-ALA135-ALA136-ASP137-THR138-ALA139-ALA140-GLN141-  
 ILE142-THR143-GLN144-ARG145-LYS146-TRP147-GLU148-ALA149-ALA150-  
 ARG151-VAL152-ALA153-GLU154-GLN155-LEU156-ARG157-ALA158-TYR159-  
 LEU160-GLU161-GLY162-LEU163-CYS164-VAL165-GLU166-TRP167-LEU168-  
 ARG169-ARG170-TYR171-LEU172-GLU173-ASN174-GLY175-LYS176-GLU177-  
 THR178-LEU179-GLN180-ARG181-ALA182-ASP183-PRO184

FIG. 11  
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FIG. 12

FIG. 12





NcoI SpeI  
 CCATGGGACACCCGAGAAACCCGGTTGTTCACTTCTTCAAAAACATCGTTACCCCGGTGAGGTGAGGCTCAGTGTGCCCCGAGGC 90  
 M G D T R E N P V V H F F K N I V T P R G G G S L V P R G  
 20 |---linker---|---thrombin---  
 TCTGGAGGTGGAGGCCACGTTTCTGTGGAGCCTAAGAGGAGTGTCAATTCTTCAATGGGACGGGTGCGGTTCCTGGACAGA 180  
 S G G G P R F L W Q P K R E C H F F N G T E R V R F L D R  
 40  
 ---linker---|  
 TACTTCTATTAACAGGAGGAGTCCGTGCGCTTCACAGCGACGTGGGGAGTTCGGGGCGGTGACGGAGCTGGGGCGGCTGACGCTGAG 270  
 Y F Y N Q E E S V R F D S D V G E F R A V T E L G R P D A E  
 80  
 TACTGGAACAGCCAGAGAGACATCCTGGAGCAGGGCGGGCGGGTGGACACCTACTGCAGACACAACACTACGGGGTGTGGAGAGCTTC 360  
 Y W N S Q K D I L E Q A R A A V D T Y C R H N Y G V V E S F  
 100  
 ACAGTGCAGCGCGAGTCATCAAGAAGAACATGTGATCATCCAGCGCGAGTTCATCTGAATCTGACCAATCAGCGGAGTTTATCTTT 450  
 T V Q R R V I K E E H V I I Q A E F Y L N P D Q S G E F M F  
 130 140  
 GACTTTGATGGTGATGAGATTTTCCATGTGGATATGGCAAGAGGACCGGTCTGGGGCTTGAAGAAATTGGACGATTGGCCAGCTTT 540  
 D F D G D E I F H V D M A K K E T V W R L E E F G R F A S F  
 160 170  
 GAGGCTCAAGGTGCATTGGCCACATAGCTGTGGACAAAGCCAACTTGGAAATCATGACAAAGCGCTCCAACCTATCTCCGATCACCBAAT 630  
 E A Q G A L A N I A V D K A N L E I M T K R S N Y T P I T N  
 190 200 210  
 XhoI  
 TAACTCGAG  
 end

FIG. 13

FIG. 14

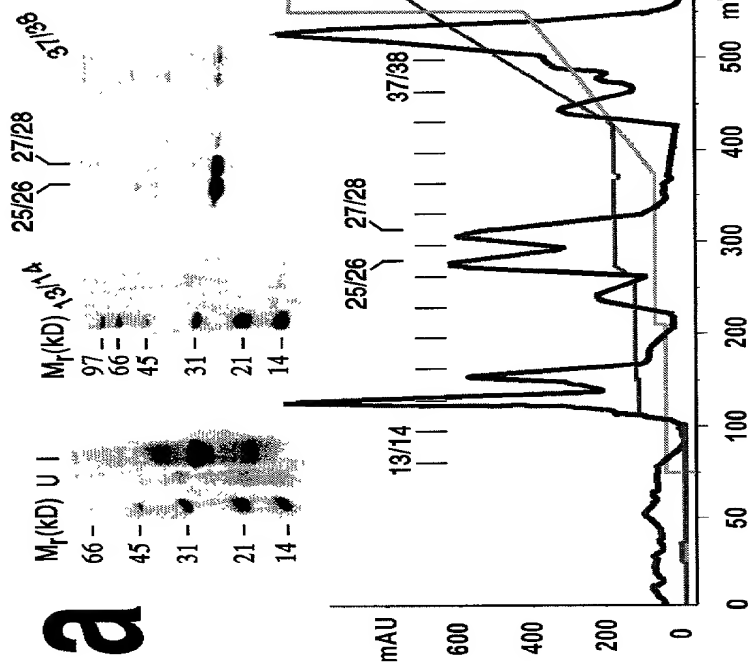
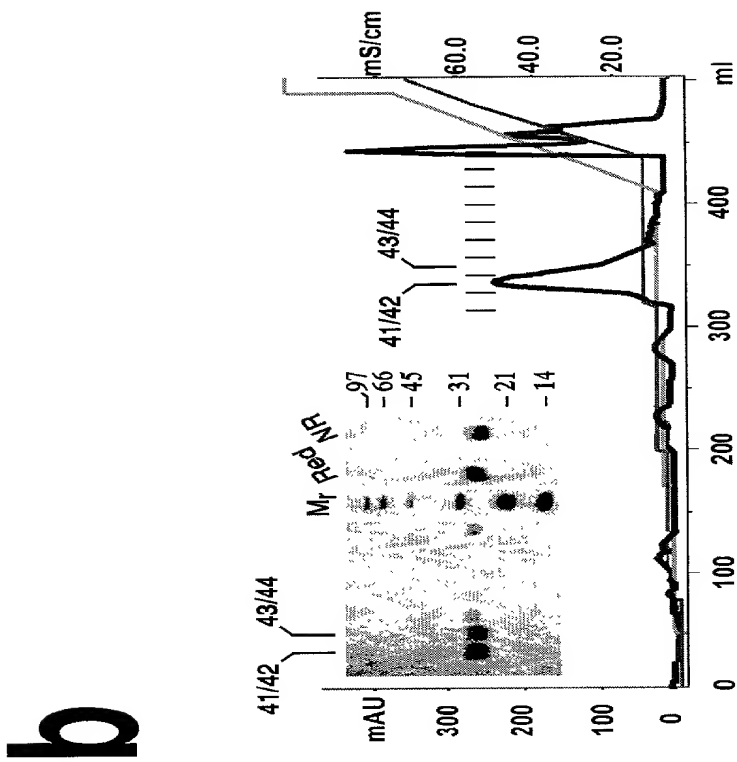
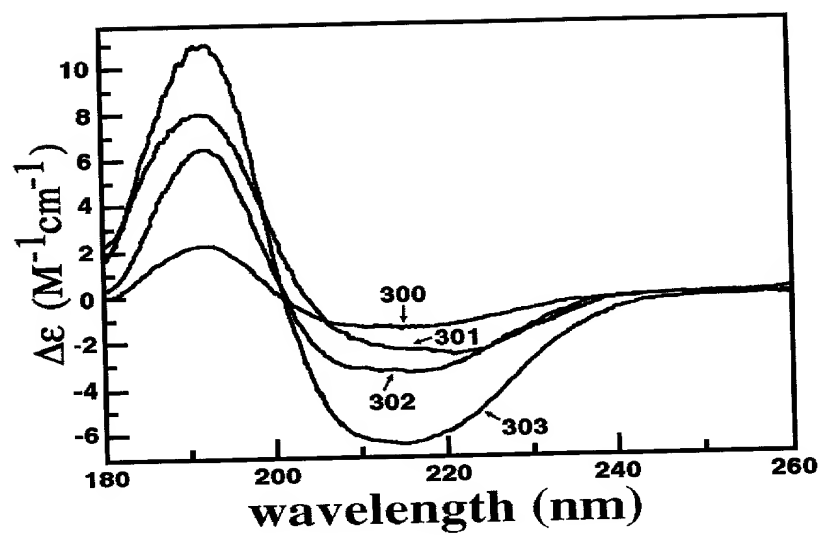


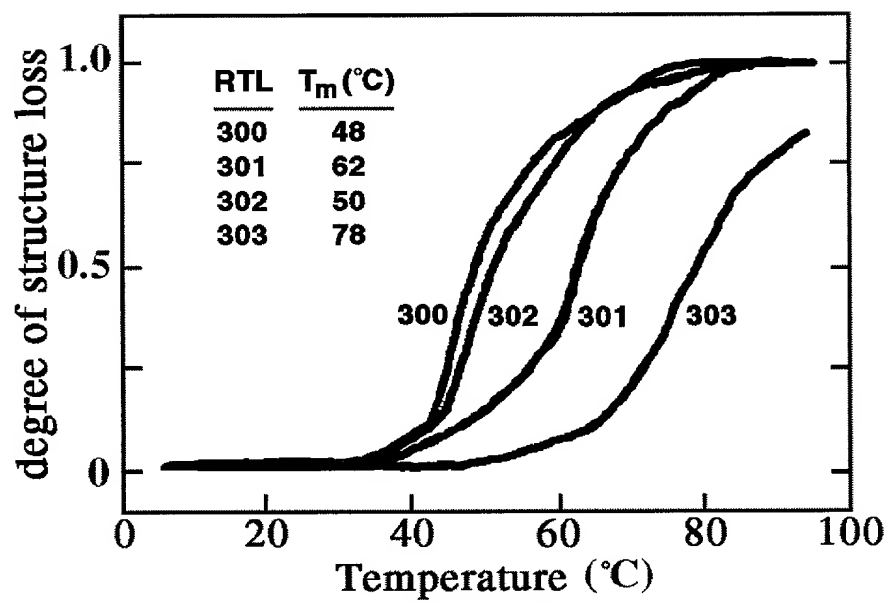
FIG. 14



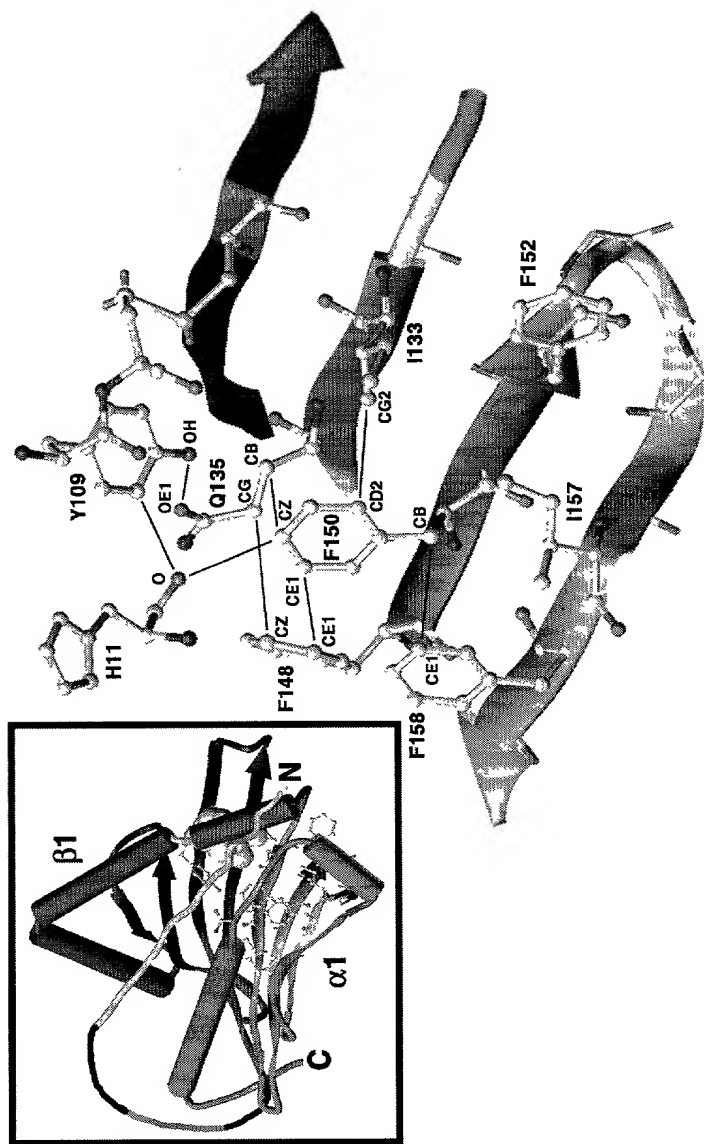




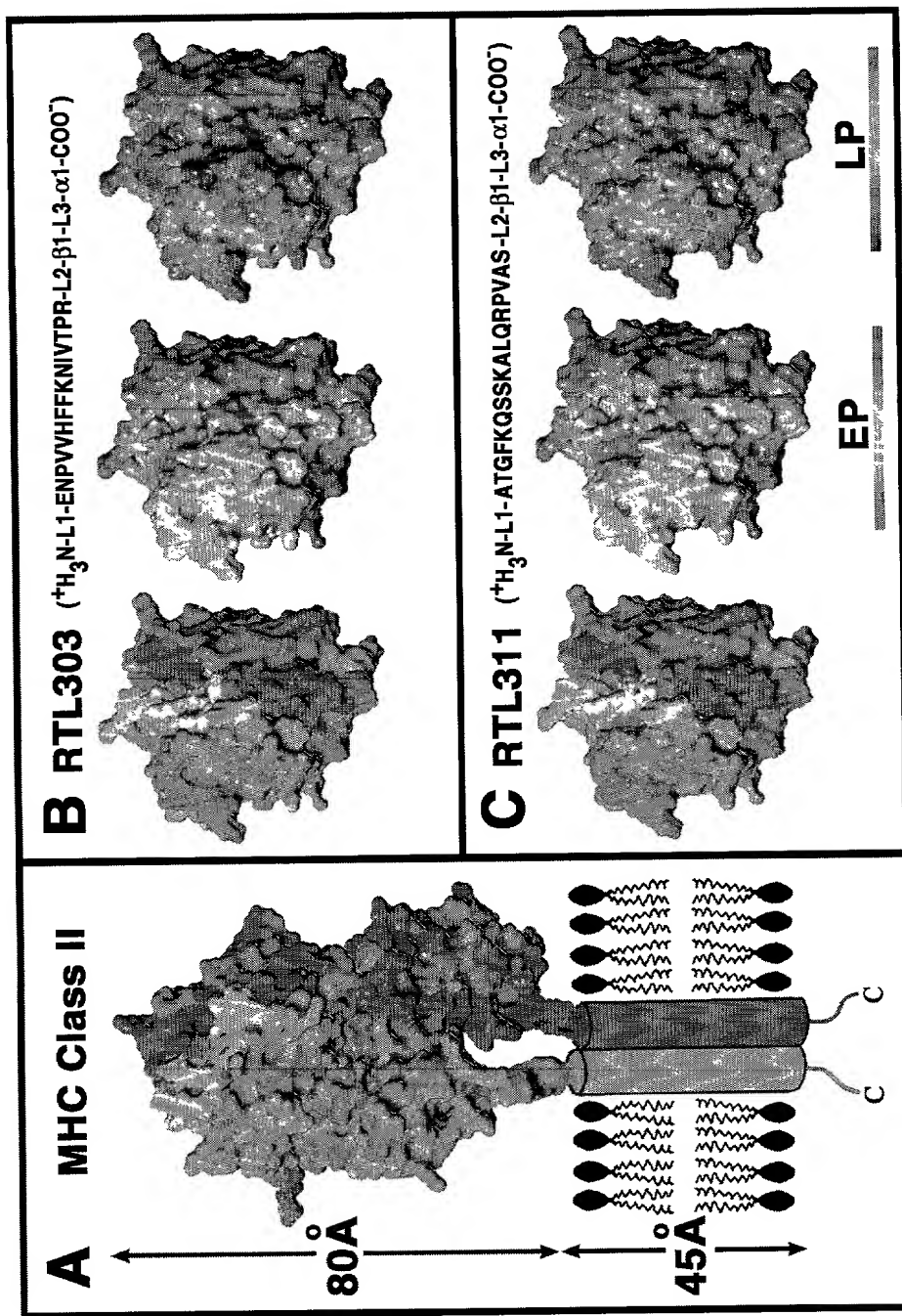
**FIG. 16**



**FIG. 17**



**FIG. 18**



**FIG. 19**

# MR#3-1 MR#2-87 CP#1-15

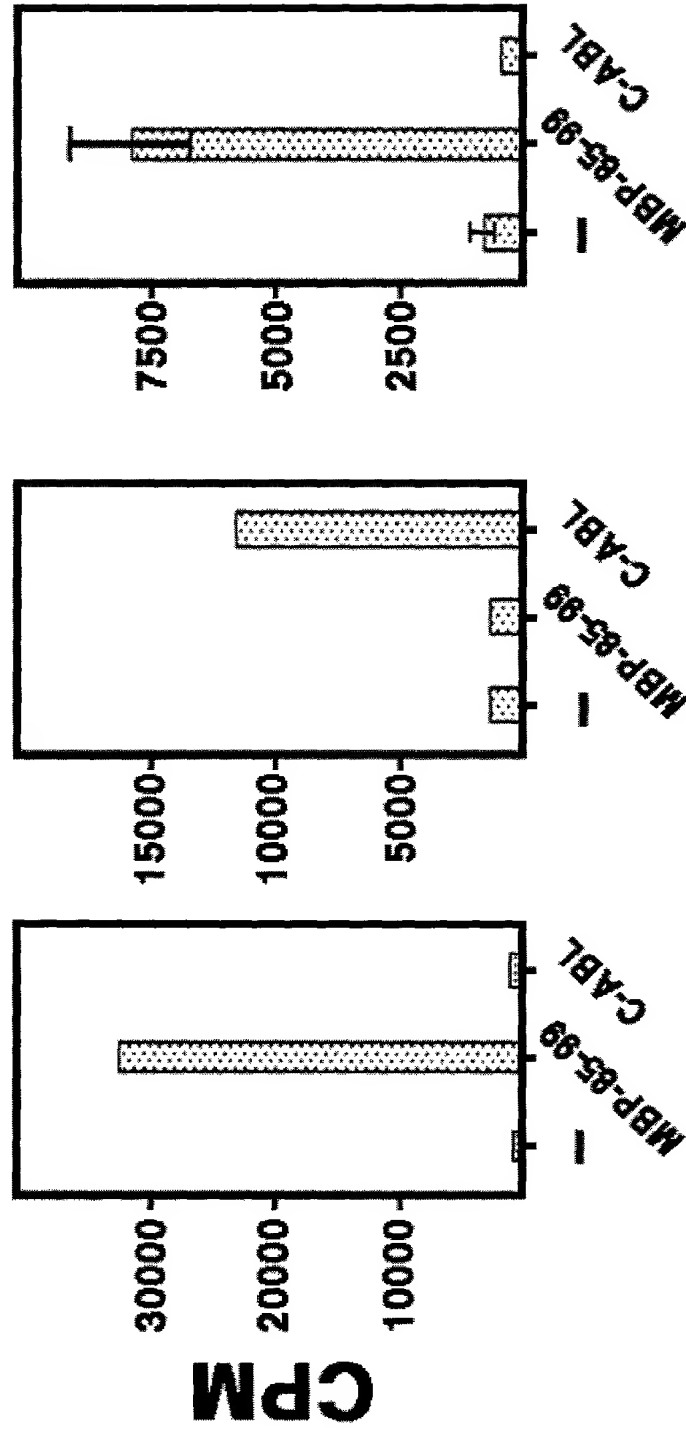
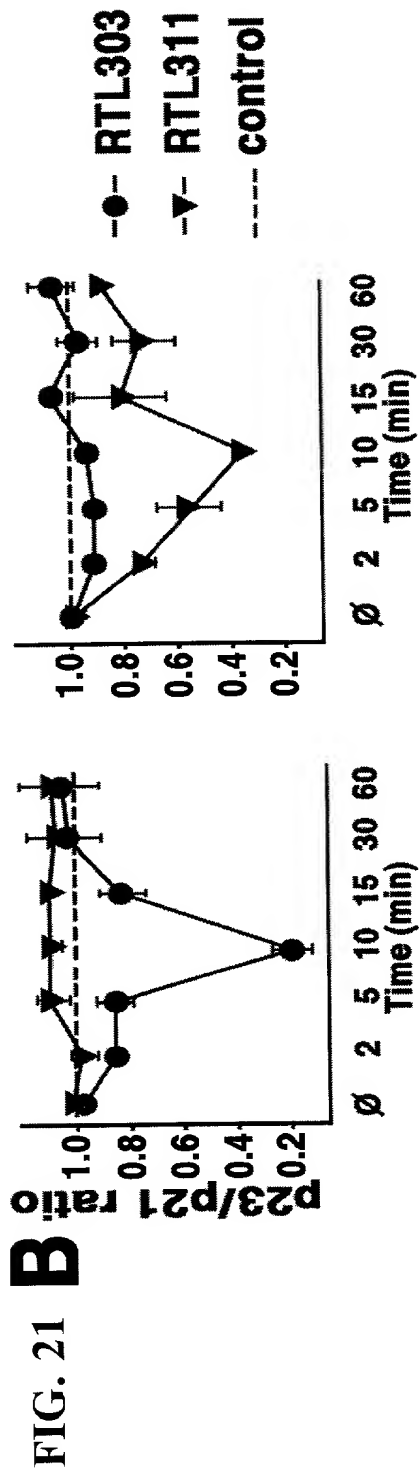
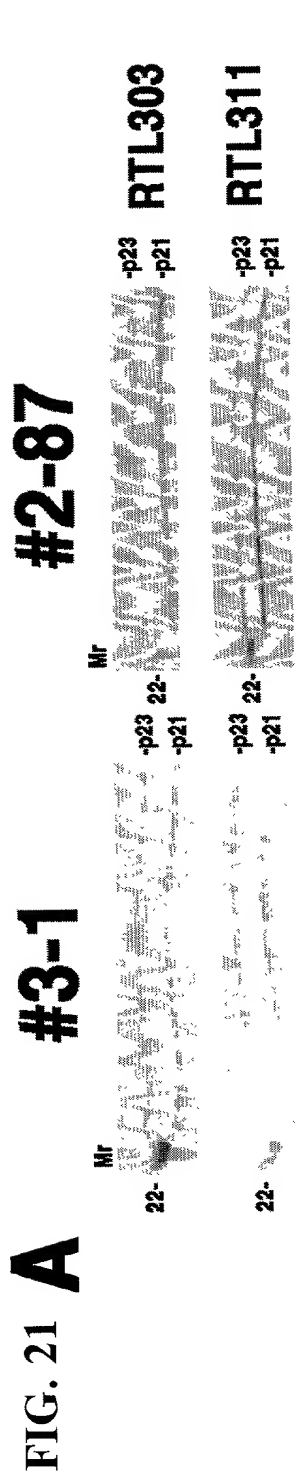


FIG. 20





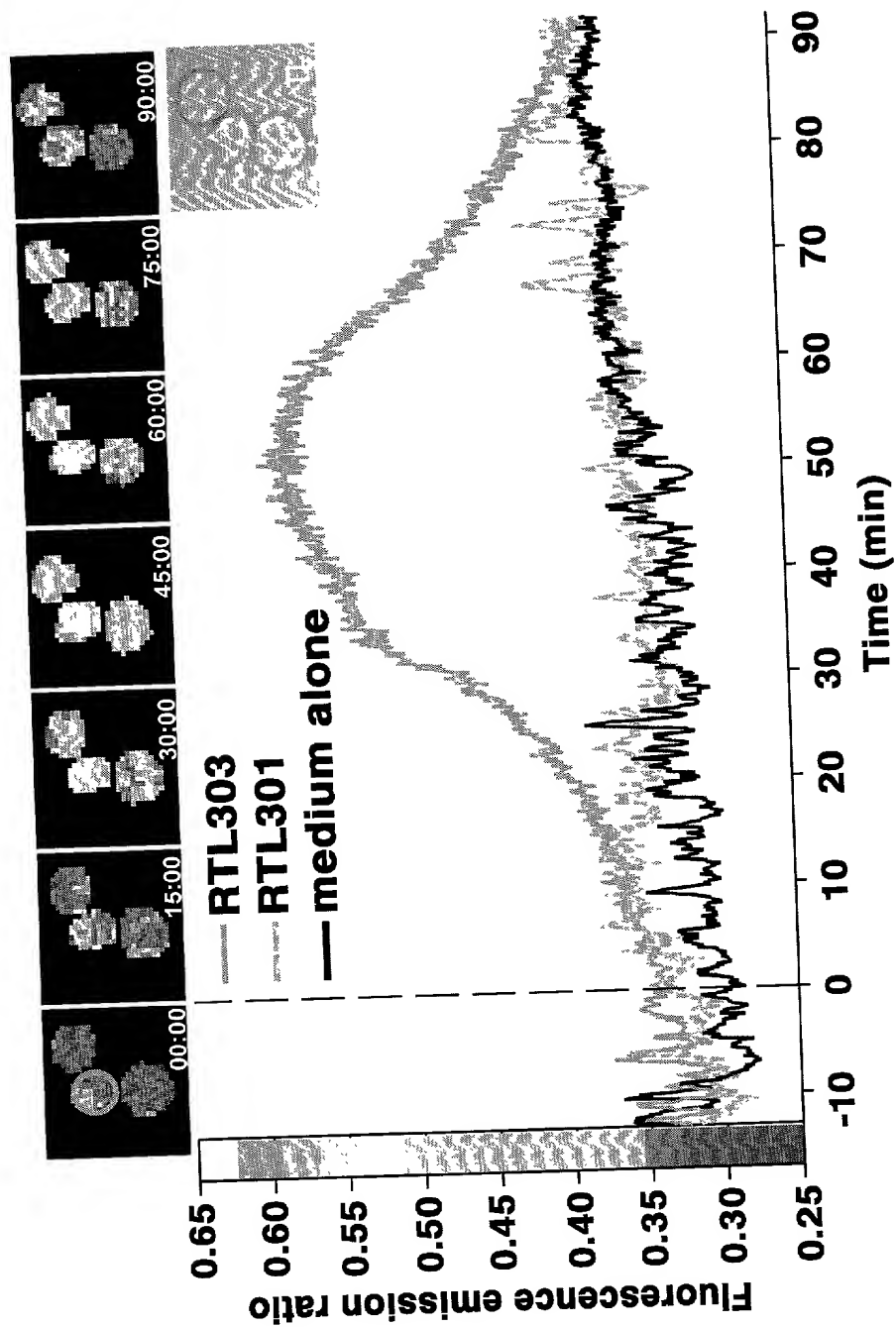


FIG. 22

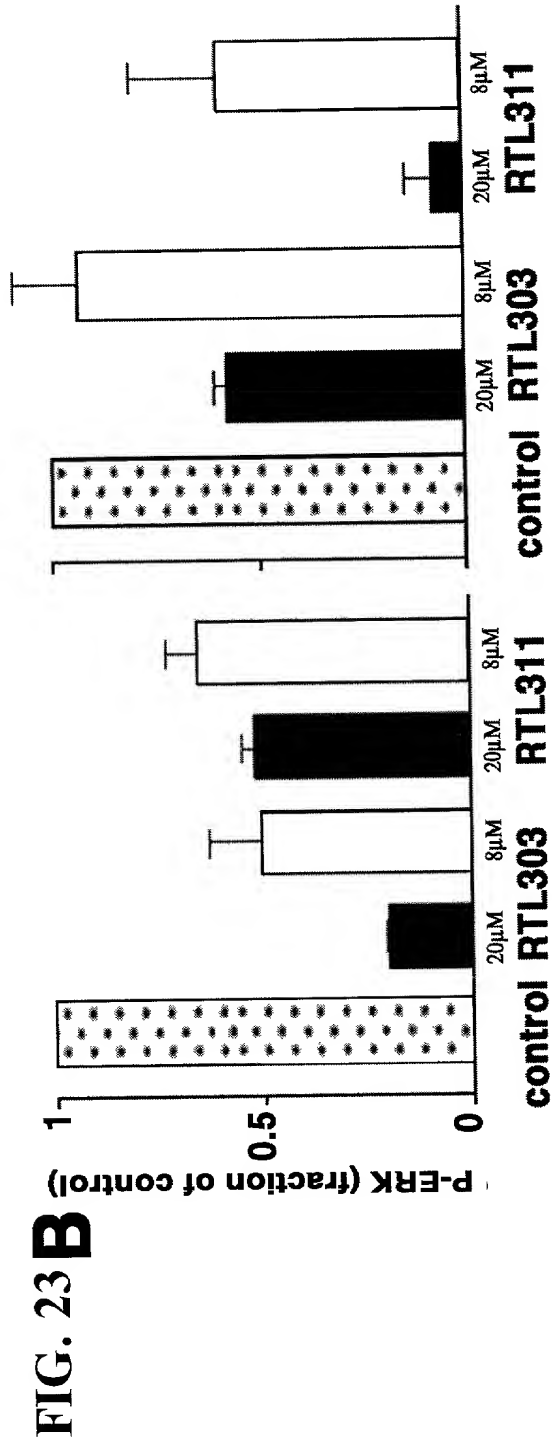
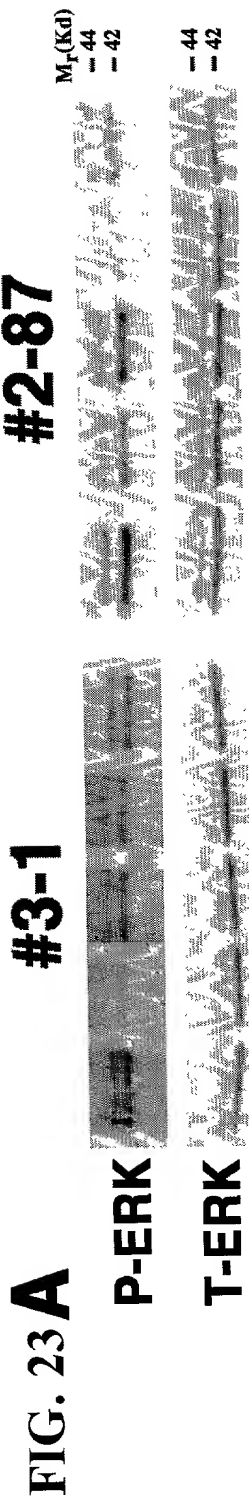


FIG. 24 A MR#3-1

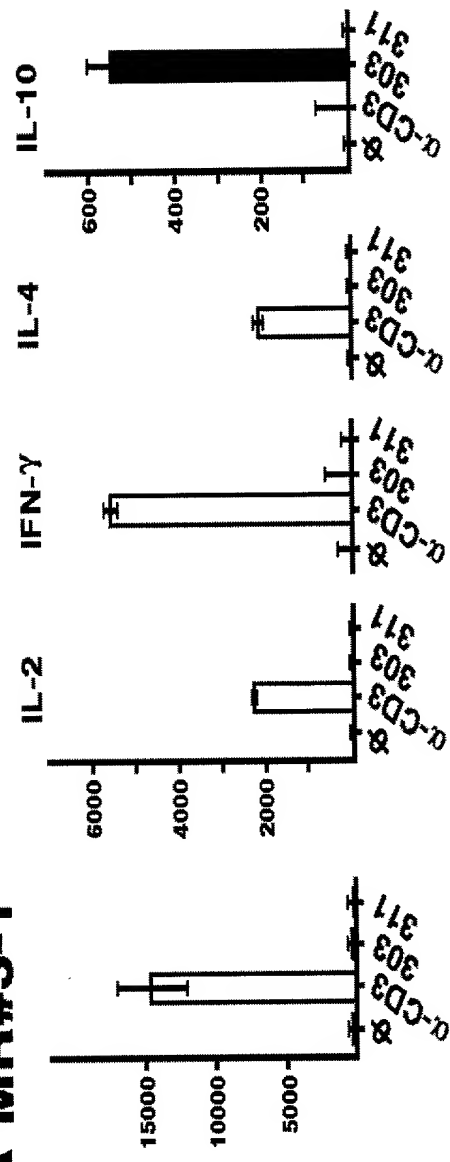


FIG. 24 B MR#2-87

